REMARKS

I. Telephonic Interview

The undersigned representative of the Applicants wishes to thank Examiner Ford for the courtesies extended during the telephone interview conducted on December 18, 2008. A summary of the interview follows.

The rejections under 35 U.S.C. §§ 112, second paragraph, 102(b) over Niklason et al. ("Niklason") in light of Hendrickson, and 103(a) over Niklason in light of Hendrickson and in view of Tu et al. were discussed.

35 U.S.C. § 112-2

The Examiner stated that it is unclear what factors were contacted with the tubular support. Agreement was reached to amend the claims essentially as follows:

"said one or more factors are comprised of:

i) one or more mitogenic factors and one or more attractant factors, and/or

ii) one or more mitoattractant factors."

35 U.S.C. § 102(b)

Claims 2, 28, 55 and 57 were discussed. The Examiner asserted that Niklason anticipates because Smooth muscle cells and endothelial cells "incorporated" in a matrix reads on the smooth muscle cells and endothelial cells "layered" on a scaffold. The Examiner stated that the scaffold is a matrix, as defined by Webster's Dictionary, and the smooth muscle cells on the scaffold also constitute a matrix into which the endothelial cells are incorporated. To distinguish over Niklason, the Examiner suggested that the method claims could be amended to recite that a "mixture" of smooth muscle cells and endothelial cells is applied to the tubular support.

The Examiner also asserted that product-by-process claim 27 and composition claims 53 and 54 recite an engineered blood vessel that is not distinguishable from Niklason.

35 U.S.C. § 103(a)

The Examiner stated that when claims are rejected for anticipation, it follows that they also are considered obvious. The Examiner also stated that claims 20 and 46 alone could have been rejected for obviousness,

but the USPTO prefers that, if all of the other claims also are rejected for anticipation, all claims be included in the rejection. The Examiner further stated that if the anticipation rejection is overcome, the obviousness rejection will be withdrawn.

II. Status of the Claims

For readability, in view of Applicants' amendments, Applicants have canceled claims 1-58 and submitted corresponding new claims 59-77. These claims all correspond to the previous claim set. Independent claim 59 corresponds to claim 2. Independent claim 68 corresponds to claim 28. Independent claim 76 corresponds to claim 55. Independent claim 77 corresponds to claim 57. The dependent claims correspond to the previous dependent claims for the previous independent claims. Accordingly, no new matter has been added with this amendment. The fact that neither smooth muscle cells nor endothelial cells are cultured with the matrix prior to combining both the endothelial cells and the smooth muscle cells with the matrix is found throughout the specification and, specifically, in the Examples, where it is clear that before both the smooth muscle cells and the endothelial cells are combined with the matrix, there is no culturing of either the endothelial cells or the smooth muscle cells with the matrix.

III. Oath and Declaration

On page 2 of the Office Action, the Examiner states that the oath or declaration is defective because it does not provide a post office address for Dr. Robert T. Tranquillo. Applicants submit an application data sheet that provides Dr. Tranquillo's post office address.

IV. The Objections

On page 2 of the Office Action, claims 2, 28, 55 and 57 are objected to for minor informalities. The new claims overcome these objections. Thus, these objections are obviated.

V. The Rejections

A. Rejection Under 35 U.S.C. §112, Second Paragraph

On page 3 of the Office Action, claims 2-6, 13, 14, 16, 20, 27 and 46 are rejected under 35 U.S.C. §112, second paragraph, on the grounds that they are indefinite. Applicants respectfully traverse the rejection.

The Examiner states that it is not clear which factors are contacted with the matrix. Accordingly, the claims have been amended to clarify the factors that are contacted with the matrix.

The Examiner further states that it is not clear if the limitations "said factors having been added to the inside of the tubular support" and "said support having allowed said factors to move from the inside of the tube to the endothelial cells in the matrix" are intended to be active steps that are carried out as part of the method, or if they are steps that were carried out prior and are not required. The newly written claims do not contain these recitations.

With regard to claims 20 and 46, the Examiner states that it is not clear which "factor" in the claims is limited to vascular endothelial growth factor. The new claims recite that the one or more mitoattractant factors is vascular endothelial growth factor. Support for this limitation is found at page 20, lines 5-7, of the specification.

In view of the above amendments, Applicants respectfully submit that all grounds for rejection have been addressed and the rejection overcome. Reconsideration and withdrawal of the rejection is, therefore, respectfully requested.

B. Rejection Under 35 U.S.C. § 102(b)

On page 5 of the Office Action, claims 2-6, 13, 14, 16, 27-32, 39, 40, 53-55 and 57 are rejected under 35 U.S.C. § 102(b) as being anticipated by Niklason et al. (Science, 1999, herein "Niklason"), in light of Henrikson (Ed.) Histology (1997). Applicants respectfully traverse the rejection.

The Examiner takes the position that chemically affixing smooth muscle cells to a PGA scaffold and then layering endothelial cells onto the smooth muscle cells at a later time constitutes incorporating these cells into a matrix. The Examiner further takes the position that by culturing the Niklason components in culture medium which, the Examiner asserts contains the claimed factors, the Niklason compositions and methods meet the limitations of Applicants' claims.

The Examiner suggests amending the claims to recite that a mixture of smooth muscle cells and endothelial cells is applied to the matrix. The unduly limits the claims. If the claims were to be amended that way, then a party could exploit the inventors' discovery and literally avoid the claims by sequentially adding the smooth muscle cells and endothelial cells to the matrix prior to exposing the combination of matrix, smooth muscle cells, and endothelial cells to the factors.

Moreover, Applicants believe that, in view of the Applicants' specification, this is not the broadest reasonable interpretation. Niklason does not teach "incorporating" smooth muscle cells and endothelial cells into a matrix. Rather, Niklason teaches attaching smooth muscle cells to chemically-modified PGA scaffolds and then culturing the Smooth muscle cells in the presence of the scaffolds. The smooth muscle cells migrate to envelop PGA fragments in the vessel lumen to form a smooth luminal surface. After an

8-week period of pulsatile radial stress, endothelial cells then are layered onto the luminal surface of the smooth muscle cells. Thus, at the very least, the endothelial cells are not incorporated into the matrix. They are layered onto the smooth muscle cells. Webster's II New College Dictionary defines the term "incorporate" as "to unite with or blend indistinguishably into an existing thing; to become united or combined into an organized body."

Although Applicants dispute the construction of the term " incorporating," to expedite prosection, Applicants have added a recitation that avoids the term and still distinguishes the claimed invention from Niklason. Applicants have amended the claims to point out that neither endothelial cells in the matrix nor smooth muscle cells in the matrix are exposed factors until both the endothelial cells and smooth muscle cells are combined with the matrix. For the compositions and methods of Niklason, the smooth muscle cells and the PGA matrix are cultured (i.e., "exposed to factors") prior to the endothelial cells being added.

In view of the above amendment, Applicants submit that all the reasons for rejection have been addressed and the rejection overcome. Reconsideration and withdrawal of the rejection are, therefore, respectfully requested.

C. Rejection Under 35 U.S.C. § 103(a)

On page 7 of the Office Action, claims 1-6, 13, 14, 16, 20, 28-32, 39, 40 and 46 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Niklason, in light of Henrikson and in view of Tu et al. (US Patent 6,506,398; herein "Tu"). Applicants respectfully traverse the rejection for the reasons below.

Applicants point out that many of the claims rejected on the grounds of anticipation are also rejected over the same prior art as being obvious over Niklason as the primary reference. The secondary references are not cited to cure the deficiencies of Niklason as to the independent claims. Henrikson is cited by the Examiner merely for its teaching that smooth muscle cells naturally secrete Type 4 collagen and Tu is cited as teaching a vascular graft having a site-specific angiogenesis factor by incorporating the VEGF and/or PDGF onto the vascular graft. As noted above in the section regarding the interview, the Examiner took the position that if a claim is anticipated then it must also be obvious. Without disputing the propriety of this statement, Applicants also point out that the Examiner indicated that if the rejection on the grounds of anticipation is overcome, then the rejection on the grounds of obviousness will fall.

The Examiner reiterates that Niklason discloses a method of producing TEBVs and anticipates the methods and compositions of claims 1-6, 13, 14, 16, 28-32, 39 and 40. The Examiner acknowledges that Niklason differs from the claimed invention in that it does not disclose inclusion of vascular endothelial

growth factor (VEGF) in the culture media. However, the Examiner submits that inclusion of VEGF in culture media for a tissue-engineered blood vessel comprising endothelial cells would have been *prima facie* obvious to one of ordinary skill in the art because the use of VEGF with tissue engineered blood vessels was well known in the art, as disclosed by Tu.

1. Discussion of Tu

Rebuttal of the rejection of claims 2-6, 13, 14, 16, 27-32, 39 and 40 has been made above in detail. Tu teaches a vascular graft having a site-specific angiogenesis factor by incorporating VEGF and/or platelet derived growth factor on the vascular graft. As such, Tu does not cure the deficiency of Niklason to teach each and every element of the claimed invention, as required by independent claims 2 and 28. Thus, because it is submitted that neither Niklason nor Tu, either alone or in combination, teaches or suggests the claimed invention as claimed in claims 2 and 28, claims 20 and 46, which depend directly from claims 2 and 26, respectively, also are deemed neither to be taught nor suggested by Niklason in light of Henrikson and in view of Tu. Reconsideration and withdrawal of the rejections is, therefore, respectfully requested.

V. Conclusion

In view of Applicants' discussion, Applicants believe that the pending claims are in condition for allowance. Early notification to that effect is respectfully requested.

Applicants believe that fees for a two-month extension of time are due with this filing. Such payment is being made simultaneously with the filing of this paper via Electronic Funds Transfer. The Commissioner is authorized to charge any deficiencies, or credit any overpayment, to our Deposit Account No. 20-0809. Applicants hereby authorizes the Commissioner under 37 C.F.R. §1.136(a)(3) to treat any paper that is filed in this application which requires an extension of time as incorporating a request for such an extension.

Respectfully submitted,

Anne Brown

Anne Brown
Reg. No. 36,463

March 23, 2008

THOMPSON HINE LLP
3900 Key Center
127 Public Square
Cleveland, OH 44114-1291
(216) 566-5715
11424957.1